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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,870	09/28/2001	Joel S. Bader	21402-135 (Cura-435)	4952
30623	7590	03/30/2004	EXAMINER	
MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C. ONE FINANCIAL CENTER BOSTON, MA 02111			SMITH, CAROLYN L	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 03/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/966,870

Applicant(s)

BADER, JOEL S.

Examiner

Carolyn L Smith

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25-27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 31102, 71703, 82203.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

Applicant's election of Group IV (claims 25-27), filed 12/22/03, are acknowledged.

Cancelled claims 1-24 and amended claims 25-27 are acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to a method of identifying regions associated with disease and predicting responsiveness to therapeutic agents, whereas in contrast the elected claims are specifically directed to a method of identifying a region associated with responsiveness to an agent.

The information disclosure statements, filed 2/11/02 and 8/22/03, have been fully considered. The information disclosure statement, filed 7/17/03, has been considered except for Cite No. C18, because this document is not a publicly published document. This international search report has been looked at by the Examiner, but it has not been officially acknowledged as being considered on its merits due to the reason given above.

Claims herein under examination are 25-27.

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Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 25-27 are rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter. One interpretation of claim 25 step (a) is that the provision of single-nucleotide polymorphisms (SNPs) involves actual laboratory practice. Another interpretation is that all steps of claim 25, including the step (a), are taking place on a computer. With this latter interpretation, the claims appear to lack any physical result performed outside of a computer.

As stated in MPEP § 2106, (IV)(B)(2)(b), to be statutory, a claimed computer-related process must either: (A) result in a physical transformation outside the computer for which a practical application in the technological arts is either disclosed in the specification or would have been known to a skilled artisan (discussed in MPEP § 2106 (IV)(B)(2)(b)(i)), or (B) be limited to a practical application within the technological arts (discussed in MPEP § 2106 (IV)(B)(2)(b)(ii)).

As stated in MPEP § 2106 (IV)(B)(2)(b)(i), the independent physical acts may be post- or pre-computer processing activity as described below:

A process is statutory if it requires physical acts to be performed outside the computer independent of and following the steps to be performed by a programmed computer, where those acts involve the manipulation of tangible physical objects and result in the object having a different physical attribute or structure. *Diamond v. Diehr*, 450 U.S. at 187, 209 USPQ at 8. Thus, if a process claim includes one or more post-computer process steps that result in a physical transformation outside the computer (beyond merely conveying the direct result of the computer operation), the claim is clearly statutory.

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Another statutory process is one that requires the measurements of physical objects or activities to be transformed outside of the computer into computer data (In re Gelnovatch, 595 F.2d 32, 41 n.7, 201 USPQ 136, 145 n.7 (CCPA 1979) (data-gathering step did not measure physical phenomenon); Arrhythmia, 958 F.2d at 1056, 22 USPQ2d at 1036), where the data comprises signals corresponding to physical objects or activities external to the computer system, and where the process causes a physical transformation of the signals which are intangible representations of the physical objects or activities. Schrader, 22 F.3d at 294, 30 USPQ2d at 1459 citing with approval Arrhythmia, 958 F.2d at 1058-59, 22 USPQ2d at 1037-38; Abele, 684 F.2d at 909, 214 USPQ at 688; In re Taner, 681 F.2d 787, 790, 214 USPQ 678, 681 (CCPA 1982).

As stated in MPEP § 2106 (IV)(B)(2)(b)(ii), the computer-related process may be limited to a practical application in the technological arts as described below:

There is always some form of physical transformation within a computer because a computer acts on signals and transforms them during its operation and changes the state of its components during the execution of a process. Even though such a physical transformation occurs within a computer, such activity is not determinative of whether the process is statutory because such transformation alone does not distinguish a statutory computer process from a nonstatutory computer process. What is determinative is not how the computer performs the process, but what the computer does to achieve a practical application. See Arrhythmia, 958 F.2d at 1057, 22 USPQ2d at 1036.

Claims 25-27 do not fulfill either of these statutory requirements and are therefore rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter.

Claims 25-27 are rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter. As written, the claims appear to be directed to a method that merely manipulates numbers, abstract concepts or ideas, or signals representing any of the foregoing.

As stated in MPEP § 2106, (IV)(B)(1), if the “acts” of a claimed process manipulate only numbers, abstract concepts or ideas, or signals representing any of the foregoing, the acts are not being applied to appropriate subject matter. Schrader, 22 F.3d at 294-95, 30 USPQ2d at 1458-59.

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Thus, a process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus cannot constitute a statutory process.

In practical terms, claims define nonstatutory processes if they:

- consist solely of mathematical operations without some claimed practical application (i.e., executing a “mathematical algorithm”); or
- simply manipulate abstract ideas, e.g., a bid (Schrader, 22 F.3d at 293-94, 30 USPQ2d at 1458-59) or a bubble hierarchy (Warmerdam, 33 F.3d at 1360, 31 USPQ2d at 1759), without some claimed practical application.

Claims 25-27 do not fulfill any of these statutory requirements and are therefore rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the

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breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF ENABLEMENT

Claims 25-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 25 recites steps (a)-(d) that provides single-nucleotide polymorphisms (SNPs) and haplotypes, identifies SNPs in at least weak linkage disequilibrium, compares these SNPs to haplotypes, and then selects a correlation test to identify a genetic region associated with responsiveness to an agent. Because steps other than step (a) do not necessarily keep the quantities of data separate between genetic regions, this lack of separation would make it difficult for one of skill in the art to be able to make and use this invention which seeks to identify a genetic region associated with responsiveness to an agent. Claim 25 does not address the scenario that more than one genetic region may form such an association. Also, if only one region is sampled as one of the options of step (a), would one of skill in the art automatically be identifying a genetic region associated with responsiveness to an agent, as stated in the last line of claim 25? To perform such a method, it appears that one of skill in the art would need to analyze any correlation test that was selected as well as use a threshold or other statistical parameter to scientifically conclude that the probability of an association significantly occurs rather than by merely selecting a correlation test and then jumping to the conclusion of region

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association identification, as stated in instant claim 25. Therefore, the steps recited in claim 25 do not appear to enable one of skill in the art to identify a genetic region associated with responsiveness to an agent.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 27 is vague and indefinite due to the unclarity of citing an abbreviation, such as ANOVA. Correction is suggested by amending in of the full name in parentheses.

Claim 25, lines 1 and 14, recite the phrase "associated with" which is vague and indefinite. It is unclear which parameters and to what degree these parameters must be met to be considered to be associated. Clarification of the metes and bounds of the claim via clearer claim wording is requested. Claims 26-27 are also rejected due to their dependency from claim 25.

Claim 25 recites the limitation "said plurality" on line 5. There is insufficient antecedent basis for this limitation in the claim as it is unclear if this phrase is referring to the plurality of single-nucleotide polymorphisms or the plurality of haplotypes in step (a). Clarification of this issue via clearer claim wording is requested. Claims 26-27 are also rejected due to their dependency from claim 25.

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Claim 25, lines 5-6, recite the phrase “at least weak” which is vague and indefinite. It is unclear which parameters and to what degree these parameters must be met to be considered to be at least weak. Clarification of the metes and bounds of the claim via clearer claim wording is requested. Claims 26-27 are also rejected due to their dependency from claim 25.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25-27 are rejected under 35 U.S.C. 102(e)(2) as being anticipated by Drysdale et al. (P/N 6,586,183 B2).

Drysdale et al. disclose a method for identifying a genetic region associated with responsiveness to β -agonists (agents) (abstract and col. 3, lines 25-36 and line 52 to col. 4, line 5). Drysdale et al. disclose a plurality of single-nucleotide polymorphisms (SNPs) in a particular region (col. 1, lines 30-67). Drysdale et al. disclose the identity of several of the polymorphic sites that are reported to be in linkage disequilibrium in a particular gene (region) (col. 2, lines 34-42). Drysdale et al. disclose a number of haplotypes for this region (col. 2, lines 42-59 and col. 4, lines 24-32). Drysdale et al. disclose determining whether additional polymorphisms exist (other regions) and how such polymorphisms are combined in different copies of the gene to

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haplotypes (col. 3, lines 25-36 and col. 5, lines 30-38) which represents the comparison step (c) of instant claim 25. Drysdale et al. disclose performing haplotyping methods on other genomic regions (col. 19, lines 50-53). Drysdale et al. disclose using various correlation techniques between a treatment and haplotypes and polymorphic sites, including regression tests and ANOVA (col. 22, lines 30-31 and col. 23, lines 7-25 and col. 24, lines 21-58). Drysdale et al. disclose analyzing haplotypes with an analysis of covariance model (ANCOVA) (haplotype-based correlation test) SNPs with an ANCOVA model (SNP-based correlation test) (col. 31, lines 1-23). Drysdale et al. disclose performing regression to determine the minimal number of polymorphisms that predict association between the polymorphisms and response to albuterol (agent) (col. 32, lines 37-40). The regression calculations created groups between haplotypes or SNPs based on response (col. 32, lines 37-45). Drysdale et al. disclosed testing sites independently (SNP-based regression) and combining sites that showed nominal association into haplotypes (haplotype-based regression) while discarding certain haplotypes with weaker associations (col. 32, lines 45-57) which represents a test selection depending on the number of SNPs in linkage disequilibrium being more or less than the number of haplotypes, as stated in instant claim 25.

Thus, Drysdale et al. anticipate the instant invention.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located

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in Crystal Mall 1. The faxing of such papers must conform to the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

March 22, 2004

Ardin H. Marschel
ARDIN H. MARSCHEL 3/24/04
PRIMARY EXAMINER